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### (54) PRODUCTION OF SOLID MATERIAL HAVING POROUS APATITE ON AT LEAST SURFACE LAYER

#### (57)Abstract:

**PROBLEM TO BE SOLVED:** To easily produce a solid having porous apatite to be utilized as an adsorbent for vital high polymer or vital org. noxious org. or inorg. ions, a medicine slow releasing carrier and a carrier of microorganisms and enzyme on at least its surface layer without allowing the material to undergo a high-temp. process.

**SOLUTION:** The calcium-contg. solid material is brought into contact with an aq. soln, contg. phosphoric acid ions and having a pH of  $\geq 7.0$ . The calcium-contg. solid material which is a starting raw material may be any among natural raw materials, such as limestone, wollastonite, shells, sea urchin shells and corals or artificial raw materials, such as calcium silicate hydrate consisting essentially of autoclave cured and formed tobermorite or lysolite, hydration cured matter of gypsum, hydration cured matter of Portland cement and hydration cured matter of alumina cement, or the raw materials formed by adding aggregate and reinforcing materials thereto. The starting raw material may be in any of powder and granular, crushed, fibrous, planar and block forms, etc.

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CLAIMS

[Claim(s)]

[Claim 1]A manufacturing method of solid matter which has a porous apatite, wherein pH contacts calcium content solid matter in 7.0 or more solution, including phosphoric acid ion on a surface at least.

[Claim 2]A manufacturing method of the solid matter according to claim 1 whose phosphoric acid ion concentration in solution is 0.1 mol / more than L (liter).

[Claim 3]A manufacturing method of the solid matter according to claim 1 in which 7.0 or more solution adds at least one sort in ammonia, sodium hydroxide, and a potassium hydrate to solution of an orthophosphoric acid, and pH adjusts pH to 7.0 or more including phosphoric acid ion.

[Claim 4]In pH, 7.0 or more solution, including phosphoric acid ion Ammonium dihydrogenphosphate, Diammonium hydrogen phosphate, a sodium dihydrogenphosphate, disodium hydrogenphosphate, A manufacturing method of the solid matter according to claim 1 which adds an alkaline substance at least one sort of solution chosen from a group which consists of potassium dihydrogen phosphate and potassium phosphate, or if needed, and adjusts pH to 7.0 or more.

[Claim 5]A manufacturing method of the solid matter according to claim 1 which is solid matter in which calcium content solid matter uses calcium carbonate as the main ingredients.

[Claim 6]A manufacturing method of the solid matter according to claim 5 whose solid matter which uses calcium carbonate as the main ingredients is limestone, a shell, a sea urchin shell, or the coral.

[Claim 7]A manufacturing method of the solid matter according to claim 1 which is solid matter in which calcium content solid matter uses a calcium silicate as the main ingredients.

[Claim 8]A manufacturing method of the solid matter according to claim 7 which is either of the calcium silicate hydrates which solid matter which uses a calcium silicate as the main ingredients generated by carrying out autoclave curing of the mixture of wollastonite (wollastonite) and lime, and silicic acid.

[Claim 9]A manufacturing method of the solid matter according to claim 1 whose calcium content solid matter is a hydrated hardened body of gypsum fibrosum, a hydrated hardened body of portland cement, or the hydrated hardened bodies of alumina cement.

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[Translation done.]

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## DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention]This invention relates to the manufacturing method of the solid matter which has a porous apatite on a surface at least. Since an apatite has chemical composition similar to the bone of a vertebrate, or the dental main ingredients and it excels in biocompatibility, are used as a bone, dental restorative dental materials, etc., but. Especially a porous thing is a material useful as a detoxication decomposition catalyst of organochlorine compounds, such as a biopolymer, living body harmful organicity or the adsorption material of inorganic ion, drugs gradual release support, support of a microorganism or an enzyme, and trichlene.

[0002]

[Description of the Prior Art]an apatite -- general formula  $A_{10}(MO_4)_6X_2$  (here -- A -- 1, such as Cu, Ba, Mg, Sr, Pb, Cd, Zn, nickel, Fe, aluminum, and La, 2, and a trivalent positive ion.) It is a general term of the mineral in which M has P, As, V, S, Si, etc., and X has the presentation of F, OH, Cl, O, etc. In this, a living body and the thing with the deepest relation are hydroxyapatite expressed with  $Ca_{10}(PO_4)_6(OH)_2$ . Hydroxyapatite is general formula  $Ca_{10}(PO_4)_6(OH)_{2-x}$  and  $nH_2O$  ( $0 < n \leq 2.5$ ,  $0 < x \leq 2.5$ ), and it is known that calcium and the (OH) basis have non-stoichiometric nature.

[0003]The apatite cured body usually sintered hydroxyapatite powder under 900-1100 \*\* and the hotpress conditions of about 10 MPa, and has obtained the cured body of about 100 MPa of compressive strength. As a manufacturing method of a porous apatite, a polymer particle is mixed to the method of using the hydraulic reaction of calcium phosphate cement, the apatite particles which carried out grain refining, or it, and shaping and the method of sintering are known. However, by manufacture of the cement powder object, by the latter, by sintering, an elevated-temperature process is needed, respectively, the problem which becomes a high cost is pointed out, and development of a simpler and cheap process is demanded at the former.

[0004]

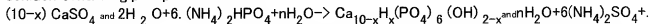
[Problem(s) to be Solved by the Invention]An object of this invention is to provide the method of manufacturing simple, without passing through an elevated-temperature process the solid matter which has at least a porous apatite used as a biopolymer, living body harmful organicity or the adsorption material of inorganic ion, drugs gradual release support, a microorganism, the support of an enzyme, etc. on a surface.

[0005]

[Means for Solving the Problem]As for a manufacturing method of solid matter which has a porous

apatite concerning this invention on a surface at least, pH contacts calcium content solid matter in 7.0 or more solution, including phosphoric acid ion.

[0006] For example, a hydrated hardened body (gypsum dihydrate) of gypsum fibrosum is converted to an apatite at the following reactions, when diammonium-hydrogen-phosphate solution is used as solution containing phosphoric acid ion.



$(4-x) \text{H}_2\text{SO}_4 + (18-x) \text{H}_2\text{O}$  — here, the first chemical formula of a product is a general rational formula of an apatite, and is  $0 < n \leq 2.5$ ;  $0 \leq x \leq 2.5$ .

[0007] As calcium content solid matter used as a starting material, Natural raw materials, such as limestone, wollastonite (wollastonite), a shell, a sea urchin shell, and coral, Or a calcium silicate hydrate which uses as the main ingredients tobermorite or a ZORITO light generated by carrying out autoclave curing of the mixture of lime and silicic acid, They may be any although aggregate and a reinforcing member were further added to artificial raw materials, such as a hydrated hardened body of gypsum fibrosum, a hydrated hardened body of portland cement, and a hydrated hardened body of alumina cement, or this. As shape of a starting material, arbitrary shape, such as the shape of a powder, the shape of debris, fibrous, tabular, and block like shape, may be sufficient.

[0008] In a generation reaction of an apatite, pH advances in 7.0 or more neutrality or a basic field. It is required to make the pH of reaction mixture high so that a pH change may not reach even acidic regions, and to increase the amount of reaction mixture. Especially if concentration of phosphoric acid ion in solution is enough to convert a part for calcium in a starting material into an apatite, are not specified, but. It is [ more than 0.1 mol / L (liter) / more than 0.5 mol / L / more than 1.0 mol / L ] preferably desirable to consider it as a range to 2.5mol/L still more preferably. When pH is less than 7.0 acidity, conversion to a perfect apatite is not obtained, but the byproduction of the stable calcium hydrogen phosphate ( $\text{CaHPO}_4$ , a mineral name: monetite) is carried out in an acidic range. However, it does not interfere that they are less than pH 7.0 acidic regions in early stages of a reaction. But it is required during a reaction to add alkali and to make pH or more into 7.0 in that case.

[0009] Although reaction temperature in particular is not limited, in order to speed up conversion reaction to an apatite, it is good to consider [ not less than 60 °C ] it as not less than 80 °C preferably.

[0010] Since reaction time changes with phosphoric acid ion concentration, reaction temperature, and porous-apatite-ized thickness of a surface request, it cannot establish a fixed standard, but it is usually a range on several from several hours.

[0011] pH including phosphoric acid ion as 7.0 or more solution, What added at least one sort in ammonia, sodium hydroxide, and a potassium hydrate to solution of an orthophosphoric acid, and adjusted pH to 7.0 or more, In or at least one sort of solution chosen from a group which consists of ammonium dihydrogenphosphate, diammonium hydrogen phosphate, a sodium dihydrogenphosphate, disodium hydrogenphosphate, potassium dihydrogen phosphate, and potassium phosphate. What added an alkaline substance if needed and adjusted pH can be used.

[0012] An apatite generated by this invention is a crystal peculiar to a 0.3 micrometer or less in thickness, and 2.0–10 micrometers in width hexagon-head tabular apatite, and a crevice between the crystal grain child is 0.5 to 0.7 micrometer of porosity.

[0013] Thus, since solid matter which has the manufactured porous apatite on a surface at least has fine pores of several micrometer order, it used various ion exchange capacity which support of bacteria, a microorganism, and enzymes and an apatite have, for example, is useful to a purifying agent, a drugs remover, etc.

[0014]When using it for the above uses, it is not necessarily required to porous-apatite-ize to a core part of calcium content solid matter which is a base, and if a surface (0.3 micrometer – about 20 micrometers) is porous-apatite-ized, it is enough in many cases.

[0015]Conversion reaction from calcium content solid matter to an apatite is a diffusion or interface reaction rate-limiting type reaction for which apatite-ization advances toward an inside from the outside of calcium content solid matter. Under the present circumstances, there is a problem of the compatibility of calcium content solid matter of a problem of generating of a stress-strain diagram in a conversion reaction process and a core part at the time of apatite-izing only a surface and a generated apatite crystal.

[0016]Since a short-time reaction may be comparatively used at low temperature (70–100 \*\*) like Examples 1–4 when apatite-izing only a surface of a particulate matter, it is not necessary to take into consideration a problem of generating of a stress-strain diagram. Although compatibility is high and has adhered with a porous apatite crystal comparatively firmly in gypsum fibrosum, portland cement, and a calcium silicate (wollastonite), adhesion is weak in limestone. on the other hand, although it was the same calcium carbonate system, by shell and a compound calcium carbonate system which contains the living thing origins, i.e., protein etc., such as husks and coral, to obtain, since an apatite crystal and a hydrogen bond which were generated on a surface were produced, it joined together firmly, and it turned out that it is stable.

[0017]In a reaction process in a case of on the other hand apatite-izing thoroughly to the depths of molding bodies, such as tabular [ larger ] than a particulate matter and block like shape, a stress-strain diagram by a density difference (specific-volume-bulk difference) by difference in a substance of both layers occurs in a reaction interface of an apatite layer and a calcium content solid matter layer of a core part. When gypsum dihydrate is used as calcium content solid matter, the density For example, apatite:  $3.21 \text{ g/cm}^3$ , Gypsum dihydrate: They are  $2.32 \text{ g/cm}^3$ , hemihydrate gypsum (drying of gypsum dihydrate generates above 100 \*\*):  $2.7 \text{ g/cm}^3$ , and anhydrous gypsum (drying of hemihydrate gypsum generates above 120 \*\*):  $2.93 \text{ g/cm}^3$ . When an interface stress-strain diagram by this density difference is large, or when it generates rapidly, a crack occurs by interfacial peeling. Therefore, it is necessary to set up appropriately reaction mixture concentration, reaction processing time, reaction temperature, and reaction mixture pH, respectively, and to advance conversion reaction. Since a reaction will be accelerated if especially reaction temperature is too high, it becomes easy to produce a crack.

[0018]

[Embodiment of the Invention]Although an example explains this invention concretely below, this invention is not limited to the following example.

[0019]

[Work example 1]Sodium hydroxide was added to the  $\text{H}_3\text{PO}_4$  solution of 2 mol / L concentration, and basic phosphoric acid aqueous solution 500mL of pH 11.0 was prepared. After holding the solution to the constant temperature bath set as 70 \*\* and reaching 70 \*\* constant temperature, about 10 g of limestone grinding things with a particle diameter of 1.0–1.5 mm were thrown in, and it was made to react for 10 hours. Filtration judgment was carried out through the after-reaction filter paper, and after distilled water washed enough, the limestone which is the particle diameter of 1.0–1.5 mm which was dried in a 100 \*\* dryer for 20 hours, and the surface apatite-ized was obtained. When this thing was observed with the scanning electron microscope, on the limestone surface, the crystal peculiar to a 0.2–0.3 micrometer in thickness and 2.0–3.0 micrometers in width hexagon-head tabular apatite was equal to the vertical direction, and was generating. The crevice between crystals was 0.5 to 0.7 micrometer, and was porosity. When the surface was mashed in

the agate mortar and having been identified according to the powder X diffraction, it turned out that it is a hydro-oxy apatite. When the powder sample which all mashed output and pulverized it with the mortar was identified according to the X diffraction, two phases of calcium carbonate and an apatite have been identified. It is limestone with this to an unreacted core part, and it turned out that the apatite plate crystal is generating the peripheral part to the vertical direction. Reaction time was lengthened further, and when it reacted for 48 hours, stirring with a magnetic stirrer in order to carry out reaction promotion moreover, it became the cloudy milky color slurry form which the apatite particles of the same particle shape distributed mostly.

[0020]

[Work example 2] The ammonia solution was added to the  $H_3PO_4$  solution of 1 mol / L, and solution 500mL of PH9.1 was prepared. After holding the solution to the constant temperature bath set as 95 °C and reaching 95 °C constant temperature, about 1 g of 1.0–1.5-mm grinding things of the shell (ark shell) were put in, and it was made to react for 4 hours. After the reaction, filtration judgment was carried out through the filter paper, and distilled water washed enough. Solid content was dried in a 100 °C oven for 2 hours. The place which contrasted the scanning electron microscope photograph before the reaction of the shell of an ark shell, and the scanning electron microscope photograph after a reaction, This reactant also checked that the 0.2–0.3 micrometer in thickness and 4–6 micrometers in width hexagon-head tubular crystal is closely located in a line with the vertical direction like Example 1, the crevice between crystals was accepted, it had a porous state apatite on a surface, and the particles whose central parts are the shells of an ark shell had been obtained. The plate crystal of the apatite was not accepted in the scanning electron microscope photograph before the reaction of the shell of an ark shell.

[0021] It has on a surface the porous apatite obtained in Example 2, and the core part carried out sterilization treatment of the 1.0–1.5-mm granular solid substance which is a shell of an ark shell at 140 °C for 2 hours. The Fermentation Research Institute mycoparasite No. (FERMP-12954: the following FERM and abbreviation) 12954 deposited with the Fermentation Research Institute, the Agency of Industrial Science and Technology, at this 0.2 % of the weight of yeast extracts, Mass culture was carried out so that shaking culture might be carried out at the number of rotations of 130 rpm for 168 hours using the liquid medium which added 0.5 % of the weight of peptone, and adjusted pH to 7.0 and it might become a  $1 \times 10^9$  individual per culture medium 1mL. This FERM shows activity to the plant pathogenic microbe of Fusarium by alkalinity by the microorganism which has antimicrobial activity. In order to investigate the microorganism support performance of the sample of Example 2, measuring and stirring 9.95 g as support, FERM of 1mL was diluted with sterilized water 1mL, and a total of two mL(s) were added. This thing was supporting FERM of the  $1 \times 10^8$  individual per 1g of support. The result of having investigated the fixing rate of immediately after incubation under [ of 38 °C ] temperature conditions, ten days, 20 days, and 30 days after for the purpose of investigating the performance of support is shown in Table 1. Thus, the performance of the obtained support was high. The shell of the ark shell of a starting material did not show support capability at all.

[0022]

[Table 1]

担持体 1 g 当りの菌数 (個)			
直後	10日	20日	30日
$1 \times 10^8$	$1 \times 10^8$	$1 \times 10^8$	$8 \times 10^7$

[0023]

[Work example 3] The potassium hydrate was added to the  $H_3PO_4$  solution of 1 mol / L concentration, and solution 500mL of PH9.3 was prepared. The solution was held at 100 \*\*, fiber diameter 150–200 micrometers of fiber length of 30–50 micrometers, and 5 g of natural wollastonite (calcium silicate) of the aspect ratios 5–7 were put in, and it was made to react for 10 hours. It dried after filtration washing like the after-reaction example 1, and the quality of a textiles shaped object of the porosity which the needlelike apatite crystal which grew up to be C shaft orientations with the shape of a needle of wollastonite held generated on the surface was obtained.

[0024]

[Work example 4] After adding and kneading water in an ordinary-portland-cement single taste and coming in shape with a particle diameter of 2.0–3.0 mm, the granular cement hardened body settled for one week was obtained. Subsequently, the ammonia solution was added to the  $H_3PO_4$  solution of 0.1 mol / L concentration, and solution 500mL of PH9.5 was prepared. The solution was set as 90 \*\*, said about 10 g of granular cement hardened bodies were supplied, and it was made to react for 8 hours. The crevice between the crystal grain children by whom the apatite hexagon-head plate crystal grew up to be a vertical direction obtained mostly about 10 g of porosity granular material which is about 5–10 micrometers on the surface of the same particle diameter after washing desiccation like Examples 1 and 2 after ending reaction.

[0025]

[Work example 5] The gypsum-dihydrate cured body of the one-side shape of about 10-mm cube (24% of porosity) When it seals to the pressure vessel made of polytetrafluoroethylene resin, and 1.70 g of drying-compression-strength 34MPa abbreviation is held for five days and made to react at 80 \*\* with about 50 mL(s) of the diammonium-hydrogen-phosphate solution (PH8.2) of 1.0 mol / L concentration, 54% of porosity, The porous body without a crack by which the core part of drying-compression-strength 11MPa was constituted from a monetite ( $CaHPO_4$ ), and the outside was constituted from an apatite was obtained. The apatite of this surface part was a porous body which has many crevices among the crystal grain children whom the apatite of the hexagon-head-like crystal generated to the vertical direction like Examples 1, 2, and 4 at the monetite of the core part.

[0026]

[Examples 6–16] The result of having changed the concentration, reaction temperature, and reaction time of diammonium-hydrogen-phosphate solution, and having processed the same gypsum-dihydrate cured body as Example 5 is shown in Table 2 with the result of Example 5.

[0027]

[Table 2]

実施例	(NH <sub>4</sub> ) <sub>2</sub> HPO <sub>4</sub> 濃度 g/L	温度 ℃	時間 日	生成物 表層／芯部	気孔率 %	圧縮強度 MPa
5	1.0	80	5	アパタイト／アパタイト	54	11
6	1.0	90	5	アパタイト／アパタイト	55	11
7	1.0	100	5	アパタイト	60	12
8	1.0	120	5	アパタイト	63	11
9	1.0	140	5	アパタイト	62	12
10	1.0	150	5	アパタイト	60	8
11	1.0	140	1	アパタイト／無水石膏	61	15
12	1.0	160	1	アパタイト／無水石膏	62	9
13	1.0	180	1	アパタイト	63	亀裂アリ
14	1.0	220	1	アパタイト	65	亀裂アリ
15	0.5	100	5	アパタイト／半水石膏	59	4
16	0.5	120	5	アパタイト／無水石膏	61	7

[0028] Examples 5-16 are the cases where the gypsum-dihydrate cured body of the one-side shape of about 10-mm cube is porous-apatite-ized. When the concentration of diammonium-hydrogen-phosphate solution is 1.0mol/L, and reaction temperature is 80 °C and 90 °C, even if it applies for five days, a core part does not apatite-ize, but if reaction temperature is not less than 100 °C, it will apatite-ize to a core part within five days. If reaction temperature is not less than 180 °C, it will apatite-ize to a core part within one day, but a crack is produced. Therefore, in order to obtain a molding body without the crack apatite-ized to the core part, it is desirable to process over many hours at the temperature of not less than 100 °C and 160 °C or less. Thus, it is thoroughly apatite-ized to a core part, and the porous apatite of block like shape which moreover has moderate compressive strength is obtained.

[0029]

[Effect of the Invention] The solid matter which has at least a porous apatite used as a biopolymer, living body harmful organicity or the adsorption material of inorganic ion, drugs gradual release support, a microorganism, the support of an enzyme, etc. on a surface can be manufactured simple, without passing through an elevated-temperature process.

[Translation done.]